



REPUBLIC OF THE PHILIPPINES  
**DEPARTMENT OF HEALTH**  
**BUREAU OF FOOD AND DRUGS**

Filinvest Corporate City  
Alabang, Muntinlupa City



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**BUREAU CIRCULAR**

No. 13-A, s. 1999

**Subject: Moratorium on the Conduct of Bioavailability/  
Bioequivalence Studies for Pharmaceutical Products  
Included in the List B' (Products with Reported  
Problems on Bioavailability/ Bioequivalence)**

1. Effective immediately, the requirement for submission of bioavailability/bioequivalence studies for pharmaceutical products included in the List B', except Rifampicin containing products, is temporarily suspended.
2. In the meantime, all applications for initial and renewal registration for products included in the List B' shall include complete data (e.g. graphs, assay methods) of comparative dissolution profiles (reference innovator product vs. product to be registered). Dissolution profiles should be performed using the following parameters:

a) Immediate release solid dosage forms

Multi - point dissolution profiles should be performed in water, 0.01N HCl, and USP buffer media at pH 4.5, 6.5 and 7.5, using either apparatus 1 at 100 revolutions per minute (rpm) or Apparatus 2 at 50 rpm for the reference product and the product to be registered (five separate profiles each). Adequate sampling should be performed at 15, 30, 45, 60, and 120 minutes until either 90% of drug from the drug product is dissolved or an asymptote is reached. The dissolution profile of the reference product and the product to be registered should be similar. Dissolution volume: 500 -1000 mL, Temperature:  $37 \pm 0.5^\circ\text{C}$ , Units to be tested: 12

b) Modified-release solid dosage forms

i) Extended release

Multi-point dissolution profiles for the reference product and the product to be registered should be performed in water, 0.01N HCl, and USP buffer media at pH 4.5 and 6.8, using either Apparatus 1 at 50, 100, and 150 rpm or Apparatus 2 at 50, 75 and 100 rpm. Adequate sampling should be performed at 1, 2, and 4 hours and every two (2) hours thereafter until either 80% of the drug from the drug product is released or an asymptote is reached. Dissolution volume: 500 -1000 mL, Temperature:  $37 \pm 0.5^{\circ}\text{C}$ , Units to be tested: 12

ii) Delayed release

Multi-point dissolution profiles for the reference product and the product to be registered should be performed in 0.01N HCl for 2 hours (acid stage) followed by testing in USP buffer media, in the range of pH 4.5 - 7.5 (buffer stage), using either Apparatus 1 at 50, 100, and 150 rpm or Apparatus 2 at 50, 75 and 100 rpm. Multi-point dissolution profiles should be obtained during the buffer stage of testing. Adequate sampling should be performed at 15, 30, 45, 60, and 120 minutes (following the time from which the dosage form is placed in the buffer) until either 80% of the drug is released or an asymptote is reached. Dissolution volume: 500-1000mL, Temperature:  $37 \pm 0.5^{\circ}\text{C}$ , Units to be tested: 12

3. All pending applications for registration of products included in the List B', except Rifampicin containing products, due to lack of bioavailability/bioequivalence data, shall now be processed.
4. The requirement for a satisfactory bioavailability/bioequivalence report, as specified under Bureau Circular No. 1, s. 1997, will resume upon notice, when bioanalytical methods are available for other products included in List B'.

For the guidance of all concerned.

  
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Director